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TECHNICAL REPORT

Demographic Variability of Inhalation Mechanics: A Review

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14. ABSTRACT

This report reviews and documents the demographic variability of inhalation mechanics in human populations, particularly with respect to the deposition of particulates in the respiratory tract. The goal is to enhance existing inhalation and respiratory mechanics models to account for population demographic variables in order to improve fidelity of casualty estimation in the Joint Effects Model (JEM) and of human effects modeling for medical planning and operational effects tools. The demographic factors influencing inhalation mechanics considered are age, gender, body size and height, ethnicity, smoking, altitude exposure, pregnancy, and lung disease. For each factor considered, relevant literature is reviewed, findings are summarized, and consequences for inhalation modeling are explored. Sample calculations using the Multiple-Path Particle Dosimetry (MPPD) model are used to demonstrate the consequences of considering demographic factors on causality estimation for a hypothetical attack scenario; it is shown that for a particle size of 3 micrometers, overall casualties will be over-predicted if the demographic factor of age is not taken into account due to differing particle deposition fractions in the lungs across age groups.

15. SUBJECT TERMS

Demographics; Particle Deposition; Inhalation Modeling; respiratory tract

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CONVERSION TABLE

Conversion factors for U.S. customary to metric (SI units of measurement)

MULTIPLY TO GET	BY BY	TO GET DIVIDE
angstrom	1.000 000 x E-10	meters (m)
atmosphere	1.012 25 x E +2	kilo pascal (kPa)
bar	1.000 000 x E + 2	kilo pascal (kPa)
barn	1.000 x E – 28	meter^2 (m^2)
British thermal unit (thermochemical)	1.054 350 x E + 3	joule (J)
calorie (thermochemical)	4.184 000	joule (J)
cal (thermochemical)/cm^2	4.184 000 x E-2	mega joule/m^2 (MJ/m^2)
curie	3.7000 000 x E + 1	giga becquerel (GBq)*
degree (angle)	1.745 329 x E – 2	radian (rad)
degree (Fahrenheit)	Tk = (t +459.69)/1.8	degree kelvin (K)
electron volt	1.602 19 x E – 19	joule (J)
erg	1.000 000 x E – 7	joule (J)
erg/sec	1.000 000 x E – 7	watt (W)
foot	3.048 000 x X-1	meter (m)
foot-pound-force	1.355 818	joule (J)
gallon (U.S. liquid)	3.785 412 x E – 3	meter^3 (m^3)
inch	2.540 000 x E -2	meter (m)
jerk	1.000 000 x E + 9	joule (J)
joule/kilogram (J/kg) (absorbed dose)	1.000 000	Gray (Gy)**
kilotons	4.183	terajoules
kip (1000 lbf)	4.448 222 x E + 3	newton (N)
kip/inch^2 (ksi)	6.894 757 x E +3	kilo pascal (kPa)
ktap	1.000 000 x E +2	newton-second/m^2 (N-s/m^2)
micron	1.000 000 x E – 6	meter (m)
mil	2.540 000 x E – 5	meter (m)
mile (international)	1.609 344 x E + 3	meter (m)
ounce	2.834 952 x E – 2	kilogram (kg)
pound-force (lbf avoirdupois)	4.448 222	newton (N)
pound-force inch	1.129 848 x E – 1	newton-meter (N*m)
pound-force/inch	1.751 268 x E + 2	newton-meter (N/m)
pound-force/foot^2	4.788 026 x E – 2	kilo pascal (kPa)
pound-force/inch^2 (psi)	6.894 757	kilo pascal (kPa)
pound-mass-foot^2 (moment of inertia)	4.214 011 x E – 2	kilogram-meter^2 (kg*m^2)
pound-mass/foot^3	1.601 846 x E + 1	kilogram/m^3 (kg/m^3)
rad (radiation absorbed dose)	1.000 000 x E – 2	Gray (Gy) **
rem (roentgen equivalent man)		Sievert (Sv) ***
roentgen	2.579 760 x E – 4	coulomb/kilogram (C/kg)
shake	1.000 000 x E – 8	second (s)
Slug	1.459 390 x E + 1	kilogram (kg)
Torr (mm Hg, 0 degrees C)	1 333 22 x E – 1	kilo pascal (kPa)

* *The Becquerel (Bq) is the SI unit of radioactivity: 1 Bq = 1 event/s.*
** *The Gray (Gy) is the SI unit of absorbed radiation.*
*** *The Sievert (SV) is the SI unit of dose equivalent.*

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PREFACE

The research work described in this report was conducted for the Defense Threat Reduction Agency (DTRA) under contract number DTRA 01-03-D-0014-0030.

The authors wish to thank Dr. Glen I. Reeves of ARA for reviewing this report and offering helpful suggestions.

1. INTRODUCTION

This report reviews and documents the demographic variability of inhalation mechanics in human populations, particularly with respect to the deposition of particulates in the respiratory tract. The goal is to enhance existing inhalation and respiratory mechanics models to account for population demographic variables in order to improve fidelity of casualty estimation in the Joint Effects Model (JEM) and of human effects modeling for medical planning and operational effects tools.

This report is divided into several sections. Section 2 provides background information related to inhalation mechanics, to include definition of critical terms. The next eight sections describe the effects of various demographic factors on inhalation mechanics. Specifically, Section 3 describes the effect of age, Section 4 describes the effect of gender, Section 5 describes the effect of body size and height, Section 6 describes the effect of ethnicity, Section 7 describes the effect of smoking, Section 8 describes the effect of altitude exposure, Section 9 describes the effect of pregnancy, and Section 10 describes the effect of lung disease. Section 11 is the conclusion to the report and Section 12 provides a list of works cited. Finally, Section 13 provides a list of abbreviations.

2. BACKGROUND

As a whole, inhalation mechanics refers to the process of breathing (1). The prime function of the lung is gas exchange; the lung allows oxygen to move from the air into the circulation and carbon dioxide to move out. Carbon dioxide and oxygen move between the air and blood by simple diffusion. The airway consists of a series of branching tubes which become narrower, shorter, and more numerous the deeper one moves into the lung. The trachea splits into the left and right main bronchi, which then divide into lobar then segmental bronchi. The terminal bronchioles are where this process ends. The terminal bronchioles are the smallest airways without alveoli. The respiratory bronchioles begin to have alveoli and connect the terminal bronchioles to the alveolar ducts, which are fully lined with alveoli.

During inspiration, air is drawn into the lung by the volume of the thoracic cavity increasing. This increase in volume is realized through both contraction of the diaphragm (which causes the lung to descend) and action of the intercostal muscles (which raise the ribs). This process is known as negative pressure breathing, as the pressure gradient caused by these actions results in the air flow. Diffusion is the primary mechanism of ventilation further down in the lung where air velocities become vanishingly small, since airway resistance increases as the airways become smaller. Inertance, which is a measure of the pressure gradient required to cause a change in flow rate with time, also changes across various sections of the lung.

Inhalation mechanics is intimately related to lung morphometry, lung volume/capacity, lung compliance and dynamic breathing parameters. There are many measures of lung morphometry and lung volume/capacity, which include parameters that are constant across all humans such as number of lobes and other basic anatomical descriptive measures, and parameters which vary, sometimes widely, due to demographics such as total lung capacity (lung volume) and tidal volume. Dynamic breathing parameters such as respiratory rate and minute volume can vary widely depending on both the anatomy of the subject and on subject activity (such as exercise). Lung compliance, which is the volume change per unit pressure change in the lung, is another factor that can differ according to demographics. For example, compliance tends to increase with age, and the compliance of the lung also depends on its size (1).

As the overall purpose of this report is to review data which may be used to enhance existing inhalation and respiratory mechanics models to account for demographics, it is worthwhile to define some common terms that appear frequently in the literature and are used to describe lung morphometry, lung volume/capacity, and other terms in the field of inhalation mechanics. Table 1 contains a listing of the most frequently encountered terms in inhalation mechanics, along with their most common abbreviations (although there can be others). An indication of whether or not the term is a parameter used in ARA's Multiple-Path Particle Dosimetry (MPPD) model is also included in Table 1.

Table 1. Commonly used measures of inhalation mechanics

Term	Common Abbreviation	Definition (according to West (1))	Used in MPPD?
Anatomic Dead Space	V_D	The volume of the conducting airways	No
Breathing Frequency or Respiratory Rate	N/A	Number of breaths per unit time	Yes

Expiratory Reserve Volume	ERV	The maximal volume of gas that can be exhaled from the resting end-expiratory level	No
Forced Expiratory Flow	FEF	The rate of airflow recorded in measurements of FVC	No
Forced Expiratory Volume	FEV	The fraction of the FVC that is exhaled in a specific number of seconds	No
Forced Vital Capacity	FVC	Vital capacity measured when the subject is exhaling with maximal speed and effort	No
Functional Residual Capacity	FRC	The volume of gas in the lung after a normal expiration (= ERV + RV)	Yes
Inspiratory Capacity	IC	The maximum volume of air that can be drawn into the lungs after a normal expiration (= TV + IRV)	No
Inspiratory Fraction	N/A	Ratio of the inhalation time to the total breathing period	Yes
Inspiratory Reserve Volume	IRV	The maximum volume of gas that can be inhaled from the resting end-inspiratory position	No
Maximum Expiratory Flow	MEF	The peak of expiratory flow as taken from the flow-volume curve (liters/second). Should theoretically be identical to PEF.	No
Minute Volume	MV or $\dot{V}$	Volume of air inhaled (inhaled MV) or exhaled (exhaled MV) from a subject's lungs in one minute (= TV x Respiratory Rate)	Yes (indirectly)
Pause Fraction	N/A	Ratio of the time spent during the pause between the inhalation and exhalation to the total breathing period	Yes
Peak Expiratory Flow or Peak Expiratory Flow Rate	PEF or PEFR	The maximal flow (or speed) achieved during the maximally forced expiration initiated at full inspiration (liters/minute)	No
Physiologic Dead Space	N/A	The volume of gas that does not eliminate CO_2	No
Residual Volume	RV	The volume of gas remaining in the lung after a maximal expiration	No
Tidal Volume	TV or V_T	The volume of air displaced during normal inspiration or expiration when extra effort is not applied	Yes

Total Lung Capacity	TLC	The volume of gas within the lungs at the end of maximal inspiration (= IC + ERV + RV = VC + RV = IRV + TV + FRC)	Yes (determined by lung geometry)
Upper Respiratory Tract Volume	URT	The volume of the respiratory tract from the nostril or mouth down to the pharynx	Yes
Vital Capacity	VC	The total exhaled volume of air (= IC + ERV)	No

Figure 1 shows a toy plot of the volume of measured air in a human lung versus time, with labels delineating various terms on the graph (these terms are defined in Table 1). Much (but not all) of the information in Figure 1 may be experimentally determined using a spirometer. The distinction "measured air" is made because the residual volume (amount of air left in lungs after maximal expiration) cannot be directly determined using a spirometer. Therefore, the red trace in Figure 1 represents only the volume of air that passes through the mouth and nose and not any residual air left in the lungs. Qualitatively, this graph shows seven normal breaths (with the differences between the upper and lower peaks defining the tidal volume), followed by one maximum inhalation and exhalation, followed by a series of more normal breaths. The relation between various terms (such as FRC = ERV + RV) may be gleaned from this figure.

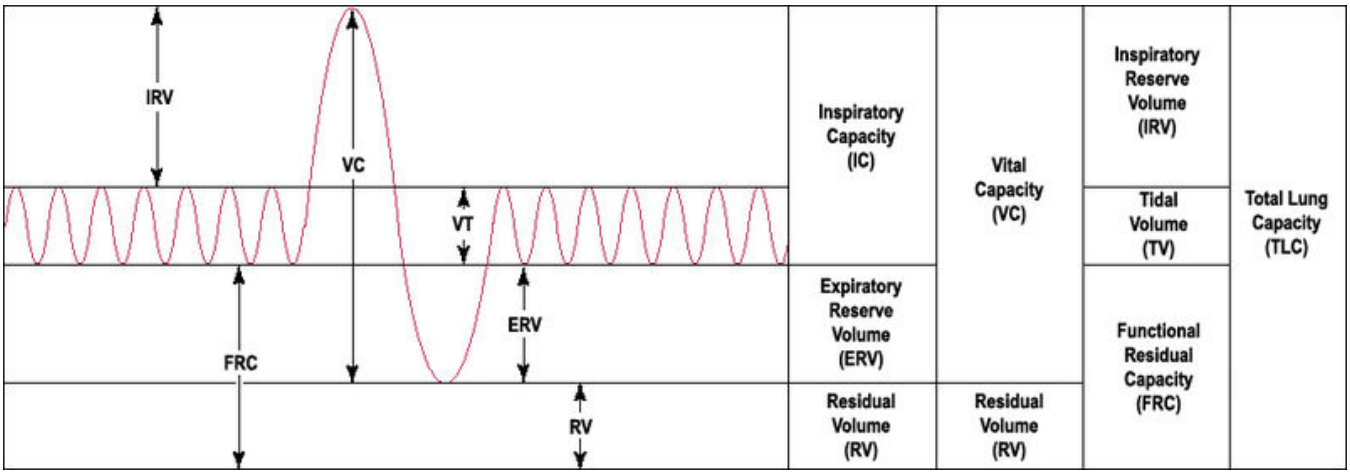

Figure 1. Graphical description of select breathing parameters (volume of measured air vs. time). See Table 1 for definition of terms

When considering demographic variability of inhalation mechanics, differences in lung geometry, lung volume/capacity, lung compliance and dynamic breathing parameters between various groups must be considered. As will be explored in the subsequent sections, there are common components that may be used to account for the observed variability in lung geometry, lung volume/capacity, lung compliance and dynamic breathing parameters. For example, Stocks and Quanjer report that body size, sex, and age are the most important determinants of lung volume (2), and that ethnic and environmental influences (such as smoking) are also important considerations. However, along with being related to lung volume, age is also an important consideration for the dynamic breathing parameter of respiratory rate (3), as adults tend to breathe at slower rates than children.

Therefore, the decision has been made in this report to consider the individual demographic factors of age, gender, body size/height, and ethnicity, as well as other elective (meaning they may not be present in all members of the population) factors of smoking, altitude, pregnancy, and lung disease, and subsequently discuss how these individual demographic factors affect lung morphometry, lung volume/capacity, lung compliance and/or dynamic breathing parameters. As a consequence of this decision, some references may be listed in more than one section due to their applicability to multiple demographic factors. The following sections follow this plan.

3. VARIATION DUE TO AGE

This section describes demographic variability of inhalation mechanics due to age. The first subsection will provide an overview of the subject, and is followed by a literature review of articles discussing variation of inhalation mechanics due to age. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

3.1. OVERVIEW

Perhaps the most intuitive effect of age on inhalation mechanics is the fact that children are generally smaller in size than adults and therefore have smaller measurements of lung descriptive parameters of interest (such as lung volume). An additional intuitive effect of age is that lung morphometry, lung volume/capacity, lung compliance and dynamic breathing parameters are expected to change as a child ages. For example, parameters such as the tidal volume and total lung capacity are expected to increase as a child ages. Some difficulty in this subject matter is present in that the only lung volume parameter that can be measured effectively in infants is the functional residual capacity (2), as an infant will not understand commands to completely inhale or exhale, which is necessary to determine the vital capacity and related parameters. The effects of puberty which are not well understood are also a confounding factor when attempting to study inhalation mechanics of pre-teen and teenage children.

3.2. LITERATURE REVIEW

Table 2 provides an overview of the literature found during the review pertaining to the effects of age on inhalation mechanics. A detailed discussion is withheld to the next subsection.

Table 2. Literature pertaining to effects of age on inhalation mechanics

Author(s)	Principal Findings
Xu and Yu (4)	Inhaled aerosol deposition in the head region is higher for children than for adults. Deposition in the tracheobronchial and alveolar regions in children can be larger or smaller than adults, depending on the particle size.
Doershuk et al. (5)	A change may occur in the relation of the size of the airways to lung volume during early infancy. Sedation may alter airway resistance.
Dunnill (6)	The number of alveoli increases over tenfold between birth and adult life, with this increase occurring mainly in the first eight years. After eight years, increase in lung volume occurs through increase in linear dimensions of existing alveoli. There is a linear relationship between the surface area of the air-tissue interface and the body surface area during the period of growth.
Hofmann (7)	Mathematical model based on experimental data developed to calculate airway parameters (such as geometrical dimensional and number of airways) as a function of age.
Phalen and Oldham (8)	Mathematical model developed to calculate inhaled particle deposition for people of various ages.
Phelan and Williams (9)	Thoracic gas volume, specific compliance, and pulmonary resistance show little difference between newborn infants and adults when related to body size.

Schibler et al. (10)	Functional residual capacity and ventilation distribution in healthy, spontaneously breathing and unsedated infants was measured and reported.
Stocks and Quanjer (2)	Reference values for residual volume, functional residual capacity and total lung capacity reported for infants, preschool children, children and adolescents, and adults based off review of literature.
Asgharian et al. (11)	Inhaled aerosol deposition fractions adjusted by inhaled air volume showed deposition was greatest for infants and decreased with age.
Meeke et al. (12)	Mean peak gas flow rates of children aged 6 and younger before and during surgery are significantly less than the mean peak flow rates before and during surgery of children more than 6 years old.
Schwartz et al. (13)	Spirometric data on 1,963 healthy subjects was analyzed. Importance of age variable decreased in older ages.
Hershenson et al. (14)	The rib cage contribution to tidal breathing of infants during quiet sleep is similar to that of adolescents by one year of age. Substantial developmental changes in rib cage shape, compliance and deformability occur during infancy.
Lapp et al. (15)	Airspace diameters correlated poorly with age and lung volumes.
Merkus et al. (16)	Growth of airways relative to lung volume occurred faster in teenage boys than in teenage girls and was compatible with isotropic growth. Subjects with respiratory symptoms in childhood and/or adolescence have lower flows for a given lung size and airway closure at a greater lung volume when they enter adulthood.
Overton and Graham (17)	An ozone dosimetry model was used to estimate regional and local uptake of ozone in the lower respiratory tract of children and adults. The total quantity of ozone absorbed per minute generally increases with age.
Phalen et al. (18)	To support predictions of inhaled particle deposition, morphometric measurements were taken on 20 replica airway casts of people aged 11 days – 21 years. The length-to-diameter ratio of growing airways did not change in any simple way as a function of airway generation.
Fleming et al. (3)	Respiratory rate declines from birth to early adolescence, with the steepest fall apparent in infants under 2 years of age.
Wallis et al. (19)	Respiratory rate declines from ages 4 to 16, with the most variation in the first three months of life. Fitted equations describing respiratory rate as a function of age are provided.
Hopper et al. (20)	Differences in lung function growth (FEV_1, VC) between girls and boys, pre- and post-puberty, showed that girls had a steadier though less pronounced increase in lung function with height. In boys, before puberty there was a deficit in lung volume relative to height which was not seen in girls.
Ménache et al. (21)	Single-path whole-lung and lobar models of the lung of children between 3 months and 21 years of age were developed based on cast data and published information. Predicted TLC for older children (8-21 years) fell within or near range from scaling equations. TLC and residual capacity volumes for children 3 years and younger need to be carefully considered for dosimetry

	modeling.
Ménache and Graham (22)	Selected descriptive statistics for 11 Mortensen casts (age 0.25 – 21 years) are discussed. Comparison of diameters among the adult lung models of Weibel (23) and Yeh and Schum (24) with two adult (18 and 21 years) males in the Mortensen (25) database are made.
James et al. (26)	Partitioning of ventilation between nasal and oral routes follows complex patterns that cannot be predicted readily by age or nasal airway resistance of the subject.
Miller (27)	Alveolar size and residual volume increase with age. TLC increases with age partly due to reduced elastic recoil.
Wu et al. (28)	Age was found to be a necessary variable for all lung function parameters explored (FVC, FEV_1, and FEF).
Boskabady et al. (29)	Age was positively correlated with pulmonary function for all variables tested (FVC, FEV_1, MMEF, PEF, VT, IRV, ERV, IC, and VC).

3.3. DISCUSSION AND RECOMMENDATIONS

A variety of important trends concerning age were observed from the literature review that should be considered in future inhalation modeling efforts. First, there is a wide variety of data pertaining to lung morpohometry and lung volume/capacity as a function of age in the literature. For example, reference values for residual volume, functional residual capacity and total lung capacity are reported for infants, preschool children, children and adolescents, and adults in Stocks and Quanjer (2), and other sources contain similar data. As noted in Table 1, functional residual capacity is an input variable for MPPD. Respiratory rate values as a function of age, which are another input into MPPD, are also found in the literature (3, 19).

The literature also contains studies that may be used to validate inhalation models. Deposition results related to age are reported in Xu and Yu (4) and Overton and Graham (17).

Overall, there is a wide range of literature concerning the effects of age on inhalation mechanics. ARA's MPPD model already incorporates the effects of age into particle deposition predictions. The available ages in MPPD (in addition to the standard adult model) are 3 months, 21 months, 23 months, 28 months, 3 years, 8 years, 9 years, 14 years, 18 years, and 21 years.

4. VARIATION DUE TO GENDER

This section describes demographic variability of inhalation mechanics due to gender. The first subsection will provide an overview of the subject. The next subsection provides a literature review of articles discussing variation of inhalation mechanics due to gender. A discussion of findings from the literature review and recommendations for inhalation modeling conclude the section.

4.1. OVERVIEW

Gender is an important consideration in inhalation mechanics due to the fact that men and women on average tend to have different body sizes, which implies that they also have different lung sizes and therefore differing values of important lung descriptive parameters. However, the expected difference between men and women when considering dynamic breathing parameters is less obvious and intuitive. Women are also different in the fact that pregnancy is a consideration; however, a discussion of the effects of pregnancy on inhalation mechanics is withheld to Section 9.

4.2. LITERATURE REVIEW

The results of the literature review of the effects of gender on inhalation mechanics are presented in Table 3. A detailed discussion is withheld to the next subsection.

Table 3. Literature pertaining to effects of gender on inhalation mechanics

Author(s)	Principal Findings
Schwartz et al. (13)	Spirometric data on 1,963 healthy subjects was analyzed. Males tended to outperform females with the same anthropometric characteristics in all age groups considered.
Martin et al. (30)	Tracheal areas in males are significantly larger than those of females even after controlling for TLC. Tracheal size in adults is unrelated to lung size across a broad range of lung sizes after controlling for sex-related differences.
Kim and Hu (31)	Particle deposition characteristics differ between healthy men and women under controlled breathing conditions. Deposition in women is greater than that in men.
Brown et al. (32)	Difference in volume variance between exhaled and inhaled boluses showed marginally significant gender effects, with volume variance between exhaled and inhaled boluses being greater in males than in females.
Carey et al. (33)	Gender plays a major role in both the healthy and diseased lung from very early life onwards. Sex hormones exert regulatory effects on lung development, physiology and pathology.
Jaques and Kim (34)	There is a differential lung dose of ultrafine particles between men and women.

Miller et al. (35)	In children, when allowing for differences in body size, forced vital capacity averaged 7% less in girls than in boys.
Hart et al. (36)	There was no significant difference between the anatomic dead space values for males and females.
Harms (37)	Women have smaller vital capacity and maximal expiratory flow rates, reduced airway diameter and a smaller diffusion surface than age- and height-matched men.
James et al. (26)	The partitioning of ventilation between the nasal and oral routes follows complex patterns that cannot be predicted readily by gender or nasal airway resistance of the subject.
Mead (38)	Women and boys have airways that are smaller relative to lung size than those of men and these sex differences develop late in the growth period.
Hoffstein (39)	Each individual tracheal area was greatest at TLC and lowest at RV, with the lung volume dependence significantly greater for men than women. A highly significant correlation between lung volume and tracheal area was found for women but not for men. In women there was good correlation between tracheal area and FEV_1 as well as maximal expiratory flow rates at 50 and 25% of VC, with these correlations being less consistent for men and depending on the lung volume at which tracheal area was measured.
Brooks et al. (40)	Men have significantly larger tracheas than women. No correlation was found for either gender between tracheal size and body size or MEF. There is a significant positive correlation between tracheal area and vital capacity in men only.
Collins et al. (41)	Airway size was not significantly different between men and women when standardized for lung size.

4.3. DISCUSSION AND RECOMMENDATIONS

The literature shows that men and women do have significant differences in some, but not all pulmonary function parameters. For example, women have smaller vital capacity, maximal expiratory flow rates, and airway diameters, but anatomic dead space values are roughly equal between the two genders. Additionally, the literature indicates that there are significant differences in the trachea between women and men. An important consideration for inspiration modeling is that experimental studies have shown that for some particle sizes, women can exhibit different deposition parameters than men (34). So, an inhalation model that distinguishes by gender should be able to predict some of these differences.

5. VARIATION DUE TO BODY SIZE AND HEIGHT

The following section describes demographic variability of inhalation mechanics due to body size and height. The first subsection will provide an overview of the subject, followed by a literature review of articles discussing the effect of body size and height on inhalation mechanics. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

5.1. OVERVIEW

Body size and height is an important consideration because when one considers two subjects that are similar in all respects (i.e. age, gender) except for body size and/or height, one would naturally expect lung volume/capacity to differ due to differences in body size and/or height. Another important consideration in terms of body size is obesity. Obesity is known to cause a scourge of health problems which can naturally be expected to affect pulmonary function.

5.2. LITERATURE REVIEW

The results of the literature review concerning the effects of body size and height on inhalation mechanics are presented in Table 4. A detailed discussion is withheld to the next subsection.

Table 4. Literature pertaining to effects of body size and height on inhalation mechanics

Author(s)	Findings
Schwartz et al. (13)	Spirometric data on 1,963 healthy subjects was analyzed. Standing height appeared to be the most important predictor of pulmonary function across the entire age group.
Naimark and Cherniack (42)	Mean compliance of the total respiratory system and particularly compliance of the chest wall was greater in normal compared to obese individuals. Total respiratory compliance was markedly reduced by recumbency in obese individuals.
Bedell et al. (43)	Obese persons had reduced expiratory reserve volumes, reduced maximal breathing capacities, and reduced maximal flow rates, and when these patients lost weight their lung function returned to normal.
Ray et al. (44)	Expiratory reserve volume changed in proportion to degree of obesity. Vital capacity, total lung capacity, and maximal voluntary ventilation only changed with extreme obesity.
Santamaria et al. (45)	In obese individuals, lung function was significantly lower in subjects that had been obese for a greater number of years
Lapp et al. (15)	Airspace diameter correlated poorly with height, weight and lung volumes.
Vilozni et al. (46)	Maximum FRC is highly correlated with height from infancy to childhood.

Hankinson et al. (47)	Mean FEV_1 increases with height for both youth and adult male and female subjects.
Hart et al. (36)	The volume of the anatomic dead space is correlated closely with height, body weight, surface area, and functional residual capacity.
Phalen et al. (18)	The tracheobronchial airways growth was describable by a linear regression on body length. Airflow rates for a given state of physical activity for various ages were found to be describable by linear regressions on body mass.
Steele et al. (48)	Measures of obesity were associated with lower lung function (FVC, FEV_1) in men and women. Waist-to-hip ratio was associated with lower lung function in men only.
Wu et al. (28)	Height was found to be a necessary variable for all lung function parameters explored (FVC, FEV_1, and FEF).
Boskabady et al. (29)	Height was positively correlated with pulmonary function for all variables tested (FVC, FEV_1, MMEF, PEF, VT, IRV, ERV, IC, and VC).

5.3. DISCUSSION AND RECOMMENDATIONS

As expected, height was found to be a major predictor of pulmonary function. The maximum FRC, mean FEV_1, tidal volume and a host of other parameters were found to be highly correlated with height. However, one item that makes interpretation of this data somewhat problematic is that many of the height studies did not control for the effect of age, which means that when implementing an inhalation model one must be careful when making the distinction between differences in function based on age versus differences in function based on height.

Obesity was also found to be an important factor in inhalation studies, principally because obesity in general causes degradation in lung function. Also, the degree of obesity is a concern, as lung volume is seen to change with morbid obesity but not with mild obesity.

6. VARITATION DUE TO ETHNICITY

The demographic variability of inhalation mechanics due to ethnicity is described in this section. The first subsection will provide an overview of why ethnicity should be a consideration, followed by a literature review of articles discussing the effect of ethnicity on inhalation mechanics. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

6.1. OVERVIEW

The effect of ethnicity on inhalation mechanics has been documented, although this subject is somewhat controversial. The major controversy stems from the fact that many researchers argue that differences due to ethnicity are principally due to differences in body size and proportions between different ethnic groups, so these confounding factors should actually be studied instead of ethnicity. There have also been social science studies that indicate that poverty and/or socioeconomic status are related to differences in inhalation mechanics due to ethnicity, although these factors are not considered here.

6.2. LITERATURE REVIEW

The results of the literature review concerning the effects of ethnicity on inhalation mechanics are presented in Table 5. A detailed discussion is withheld to the next subsection.

Table 5. Literature pertaining to effects of ethnicity on inhalation mechanics

Author(s)	Findings
Schwartz et al. (13)	Spirometric data on 1,963 healthy subjects was analyzed. Controlling for other variables, African-Americans exhibited consistently lower respiratory function for most measures.
Hankinson et al. (47)	Caucasian subjects had higher mean forced vital capacity and forced expiratory volume at one minute than Mexican-American and African-American subjects across the entire age range. Caucasian and Mexican-American subjects had similar FVC and FEV_1 values with respect to height, and African-American subjects had lower values.
Whittaker et al. (49)	Ethnicity was an independent predictor for all lung function measures except PEF. FVC in Whites was 13.4% bigger than Asians of the same height. FEV_1 was 10.6% greater in Whites compared to Asians.
Lapp et al. (50)	Total lung capacity and residual volume of African-Americans are decreased by approximately 12% compared to Caucasians of the same age and height. Expiratory flow rates were similarly decreased but were not significant when TLC was matched.
Quanjer et al. (51)	Based on trends in the FVC, it is likely that lung volumes in Polynesians, Northern Indians, and Pakistanis are 10% smaller than in Caucasians.
Miller et al.	Allowing for differences in body size, forced vital capacity averaged 16% greater in children of European origin than in children of African descent. The lung size of persons

(35)	of mixed racial origin is intermediate between that of the parents.
Donnelly et al. (52)	Caucasian subjects had mean total lung capacity and vital capacity that was 5% higher than Chinese subjects and 20% higher than Indian subjects. Chinese values for these measurements were 12% and 10% greater than Indian values.
Harik-Khan et al. (53)	African-Americans have lower lung function than Caucasians, and this difference is only partially explained by a shorter upper body segment in African-Americans.
Kiefer et al. (54)	The mean lung function for a given age, gender, and height was the same for Caucasians and Mexican-Americans but was lower for African-Americans.
Yang et al. (55)	As predicted normal values are widely used for routine assessments, it is important that the noted differences in lung volumes between the races are recognized.
Korotzer et al. (56)	Asian values for forced vital capacity, forced expiratory volume in 1 second, and alveolar volume were significantly lower than for Europeans.
Pool and Greenough (57)	When comparing Caucasian and Afro-Caribbean children, no significant differences were found in PEFR, and FRC was greater in Caucasian children when related to standing but not sitting height.

6.3. DISCUSSION AND RECOMMENDATIONS

The literature has shown that ethnicity is an important consideration for inhalation mechanics. One important note is that most inhalation models in use today are based on Caucasian subjects. Hankinson et al. (47) noted that there were differences in body build due to ethnicity. They attributed these differences to body size and proportions, arguing that Mexican-Americans were shorter than Caucasian subjects of the same age, and African-Americans had on average smaller trunk to leg ratios than Caucasians. However, in contrast to this body proportions argument, Whittaker et al. (49) noted that differences in chest dimensions did not explain the substantial effect of ethnicity on lung function when comparing Caucasians and Asians. They instead argued that differences in inspiratory muscle strength or lung compliance may explain differences in ethnicity lung function but noted that this assertion remains speculative.

Donnelly et al. (52) noted that Caucasians had higher fat free masses, higher inspiratory and expiratory muscle pressures, and wider chests than Chinese and Indian subjects. Caucasian and Chinese subjects also had longer chests than the Indian subjects. They conclude that Caucasians had larger lung volumes than Chinese and Indians because they have increased numbers of alveoli and physically larger chest cavities, and not because of greater alveolar distensibility.

Further research must be conducted to determine the exact procedure for accounting for ethnicity in inhalation models. The literature suggests that certain parameters such as lung volume may be directly related to ethnicity, but other parameters that differ by ethnicity may be a result of height or body size differences. Another difficultly is determining how to define the ethnic groups, and the closely related question of how many ethnic groups can be defined and differentiated in terms of inhalation mechanics parameters with statistical justification based off of the available data.

7. VARIATION DUE TO SMOKING

The demographic variability of inhalation mechanics due to smoking is described in this section. The first subsection will provide an overview of why smoking should be a consideration, followed by a literature review of articles discussing the effect of smoking on inhalation mechanics. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

7.1. OVERVIEW

Smoking is known to have a variety of negative health effects, and given the fact that smoking of course involves inhaling toxic particles into the lungs, may be reasonably expected to affect pulmonary function. Smoking differs from previously discussed factors in that it is elective, meaning that some members of the population may choose to start (or stop) smoking at random times, and many will never smoke at all in their lives. So, smoking can be present or absent at unpredictable periods of time for selected members of the population. However, response planners in an urban area can predict what percentage of the population at a given time does smoke, so it is a worthwhile endeavor to account for the effect of smoking on inhalation mechanics.

7.2. LITERATURE REVIEW

Table 6 provides the results of the literature review pertaining to the effects of smoking on inhalation mechanics. Discussion is withheld to the next subsection.

Table 6. Literature pertaining to effects of smoking on inhalation mechanics

Author(s)	Findings
McCawley and Lippmann (58)	Dispersion of a 0.5 micron aerosol bolus during tidal breathing is significantly greater for smokers compared to non-smokers after matching for gender and age.
Hensler and Giron (59)	Smokers were found to have significantly lower average ventilatory capacities and increased residual volumes compared to nonsmokers. Smokers tended to exhibit abnormal results to tests of maximum voluntary ventilation, timed VC, and RV compared to nonsmokers.
Apostol et al. (60)	Smoking causes an increased rate of decline of FEV_1 with age.
Awan and Alphonso (61)	Smokers exhibited significantly lower vital capacities compared to non-smokers.
Wang et al. (62)	Current and cumulative cigarette smoking were significant predictors of reduced maximal level of FEV_1 in males but not in females.
Chamberlain et	Central deposition of particles increased at higher respiratory rates, especially for

al. (63)	smokers.
Nagelmann et al. (64)	Chronic smokers showed a significant reduction of forced expiratory volume in 1 second and reduction of airway specific conductance

7.3. DISCUSSION AND RECOMMENDATIONS

Smoking is seen to affect a variety of inhalation mechanics parameters such as residual volume, vital capacity, and aerosol dispersion. Implementing the effect of smoking into an inhalation model would require considering degradation of pulmonary function, and the results should be evident in deposition characteristics. An area for future study is the effect of amount of smoking on inhalation mechanics, as a two-pack-per-day smoker may or may not have different pulmonary function than a subject that smokes a smaller number of cigarettes per day.

8. VARIATION DUE TO ALTITUDE EXPOSURE

The demographic variability of inhalation mechanics due to altitude exposure is described in this section. The first subsection will provide an overview of why altitude exposure should be a consideration, followed by a literature review of articles discussing the effect of altitude on inhalation mechanics. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

8.1. OVERVIEW

The effects of altitude on pulmonary function stem from the fact that air at altitude is thinner (both barometric pressure and the partial pressure of oxygen fall), and therefore a person that breathes air at altitude is not able to obtain the same amount of oxygen per unit volume of air than someone at sea level. It is known that people are able to acclimatize to thinner air at altitude after a certain amount of time, but the focus here will be on people that are born and raised at altitude, as long-term altitude exposure during growth will have a much greater effect on inhalation mechanics as biological adaption to the higher altitude will occur. As with smoking, altitude exposure may be viewed as elective, since not all members of a population will have been raised in a high-altitude environment.

8.2. LITERATURE REVIEW

Table 7 summarizes the results of the literature review pertaining to the effects of altitude on inhalation mechanics. Discussion is withheld to the next subsection.

Table 7. Literature pertaining to effects of altitude on inhalation mechanics

Author(s)	Findings
Vinnikov et al. (65)	Work at high altitude for years may be a factor that accelerates lung function (VC, FVC, and FEV_1) decline.
Greksa (66)	Growth at high altitude results in an enhancement of lung volumes (particularly residual volume), which is 70-80% greater in highland than in lowland children.
Weitz et al. (67)	Growth at high altitude produces small-to-moderate increases in lung volumes (about 6%) relative to genetically similar groups growing up at low altitude.
Agostoni et al. (68)	At high altitude, lung diffusing capacity improves with acclimatization due to increases in hemoglobin, alveolar volume and membrane diffusion.
Palmer (69)	Acclimatization describes the physiologic changes that help maintain tissue oxygen delivery and human performance in the setting of hypobaric hypoxemia. These changes include a marked increase in alveolar ventilation, increased hemoglobin concentration and affinity, and increased tissue oxygen extraction.

8.3. DISCUSSION AND RECOMMENDATIONS

The literature review indicates that a necessary requirement of increased lung volume due to altitude is that the person is born and raised at high altitude. A person who is born and raised at sea level then moves to high altitude does not see increased lung volume, although acclimatization does result in increases in alveolar volume. One study indicated that a sea level person that moves and works at altitude will exhibit declined lung function.

Implementing the effects of altitude into an inhalation mechanics model for a person born and raised at altitude would be relatively straightforward, as lung geometry parameters would simply have to be adjusted. The much more difficult problem would be consideration of a sea level acclimatized person that moves to altitude. Additionally, when implementing an inhalation mechanics model, the fact that the properties of air at altitude (i.e., density and composition) are different must be considered. Most notably, variations in the properties of ambient air will affect the behavior of aerosols.

9. VARIATION DUE TO PREGNANCY

The demographic variability of inhalation mechanics due to pregnancy is described in this section. The first subsection will provide an overview of why pregnancy should be a consideration, followed by a literature review of articles discussing the effect of pregnancy on inhalation mechanics. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

9.1. OVERVIEW

Pregnancy is a consideration for inhalation mechanics because physiologically, the diaphragm is compressed by the uterus during pregnancy, which is expected to have an effect on breathing parameters. Oxygen intake to support the fetus is also a consideration, which would be expected to have an effect on dynamic breathing parameters. Pregnancy is a unique parameter to consider with respect to inhalation mechanics because 1) it only applies to females, and 2) its effect is only present for a relatively short, well-established time period (i.e., nine months). However, response planners in an urban area will be able to estimate what portion of the population is pregnant at any given time; therefore considering the effect of pregnancy on inhalation mechanics is an important factor to consider.

9.2. LITERATURE REVIEW

Table 8 describes the literature reviewed pertaining to the effects of pregnancy on inhalation mechanics. Discussion is withheld to the next subsection.

Table 8. Literature pertaining to effects of pregnancy on inhalation mechanics

Author(s)	Findings
McAuliffe et al. (70)	For pregnant women at sea level, RV and TLC were higher in the third compared with the first trimester. At high altitude, FEV_1, ERV, and FRC were lower in the third compared with the first trimester.
Hegewald and Crapo (71)	Important respiratory system changes occur in the upper airway, chest wall, static lung volumes, and ventilation and gas exchange during pregnancy.
Russell and Chambers (72)	A decrease in functional residual capacity as pregnancy progressed resulted in airway closure during tidal breathing in more than 50% of subjects at term when in a supine position, but this decrease did not occur when they were seated.
Garrard et al. (73)	No consistent changes in lung volume could be shown during pregnancy, although closing volume was found to increase during pregnancy.
Alaily and Carrol (74)	Major changes in tidal volume, functional residual capacity and residual volume were seen during pregnancy. Minor changes were found in many other measurements, all of which occurred at an early stage of pregnancy.

9.3. DISCUSSION AND RECOMMENDATIONS

One interesting finding from the literature review pertaining to pregnancy is that the stage (trimester) of pregnancy is an important consideration, which has implications for modeling efforts. Pregnancy was found to change tidal volume, functional residual capacity and residual volume, although interestingly not lung volume.

10. VARIATION DUE TO LUNG DISEASE

The demographic variability of inhalation mechanics due to lung disease is described in this section. The first subsection will provide an overview of why lung disease should be a consideration, followed by a literature review of articles discussing the effect of lung disease on inhalation mechanics. A discussion of findings from the literature review and recommendations for inhalation modeling concludes the section.

10.1. OVERVIEW

Lung disease is a consideration for inhalation mechanics because lung disease is expected to negatively affect functioning of the pulmonary system. Common lung diseases include emphysema, asthma, pulmonary fibrosis, and chronic obstructive pulmonary disease (COPD). Lung disease is selective in that it will only be experienced by a low proportion of the population, and may or may not be present at all times.

10.2. LITERATURE REVIEW

Table 9 describes the literature reviewed pertaining to the effects of lung disease on inhalation mechanics. Discussion is withheld to the next subsection.

Table 9. Literature pertaining to effects of lung disease on inhalation mechanics

Author(s)	Findings
West (1)	Asthma is an obstructive disease which reduces FEV_1 and causes the flow rate to be very low in relation to lung volume. Pulmonary fibrosis is a restrictive disease which reduces FEV and FVC, and reduces the maximum flow rate and total volume exhaled.
Hogg (75)	COPD is defined by airflow limitation, which is caused by increased resistance of the small conducting airways and increased compliance of the lung as a result of emphysematous destruction.
Hogg (76)	COPD causes FEV_1 decline. Emphysematous destruction of the gas exchanging tissue also contributes to the airflow limitation by reducing elastic recoil pressure available to drive air out of the lung during forced expiration.
Tuft and Blumstein (77)	There is a reduction of vital capacity during asthmatic seizures and a return to normal in symptom-free intervals. Epinephrine is used to increase the vital capacity during asthmatic seizure.
Nagelmann et al. (64)	Cigarette smoking causes airflow limitation with lung hyperinflation being the primary causes of COPD.
Fowler (78)	The mean respiratory dead space of nine patients with emphysema was significantly greater than the mean value for young men. The tidal volume of patients with emphysema was smaller when breathing pure oxygen than with air.

Apiou-Sbirlea et al. (79)	The effect of diseases on aerosol deposition was modeled by simulating constrictions and blockages. Respiratory diseases may influence the deposition of inhaled drugs in a systematic and predictable manner.

10.3. DISCUSSION AND RECOMMENDATIONS

As expected, lung disease is unilaterally associated with a decrease in lung function. One difficulty with modeling the effects of lung disease in inhalation models is that fact that some (but not all) lung diseases are associated with smoking, so the effects of the disease must be decoupled from the effects of smoking. Additionally, COPD is defined as the co-occurrence of chronic bronchitis and emphysema, so a distinction must be made between subjects that have emphysema only versus COPD.

11. APPLICATION OF DEMOGRAPHIC VARIABILITY OF INHALATION MECHANICS TO FUTURE MODELING EFFORTS

A common theme throughout this review is the potential for application of inhalation mechanics demographic data to future modeling efforts. Taking demographics into account when conducting modeling will enable more accurate predictions of factors of interest including both effects on individuals and casualty estimation for populations as a whole. The purpose of this section is to explore some ideas related to application of demographic variability of inhalation mechanics to future modeling efforts.

11.1. OVERVIEW

As they stand today, programs that predict casualties from a chemical/biological attack on a population usually assume a "typical" person, for example an adult of certain age and sex. Furthermore, many of the inhalation models based on experimental data may be biased due to the data used to formulate the models; for example, it was noted in the section on ethnicity that an overwhelming majority of the experimental data collected to date has used Caucasian subjects.

For some applications, using a "typical" subject may be a reasonable assumption. This assertion is especially true when dealing with predicting the effects of an attack on a military population. As a whole, military populations are all adult, in most cases are overwhelmingly male, and reasonable assumptions may be made concerning the age of the military population (i.e., at the least 18 years old and at the most 55-60 years old, with age numbers biased towards the lower end of the age spectrum).

However, there are applications where assuming the population is uniform is problematic. Predicting the effects of an attack on a civilian population is one such example. Civilian populations are widely varied in parameters such as age, sex, ethnicity, height/weight, and other factors discussed in this document. Thankfully, there are methods by which population variability may be accounted for in casualty prediction models. One such way to account for population variability is use of US Census data. The US Census Bureau publishes detailed data (80) concerning demographic factors of the population that may be used to characterize a population as a whole. Of course, there is still potential for significant variation in population by city, as some cities may tend to have older populations while others may tend to have younger populations.

The next two sections will explore some consequences of accounting for a demographic variable, in this case age, when formulating casualty predictions based on inhalation models.

11.2. SAMPLE MPDD CALCULATIONS

As mentioned in the previous section discussing demographic variability of inhalation mechanics due to age, MPPD already incorporates the effects of age into particle deposition predictions. The available ages in MPPD in addition to the standard adult model are 3 months, 21 months, 23 months, 28 months, 3 years, 8 years, 9 years, 14 years, 18 years, and 21 years.

To illustrate the effects of age on particle deposition, MPPD simulations were run to give a baseline comparison. The parameters available for use in the simulations are listed in Table 10.

The effect of incorporating an age model in MPPD is that the parameters of FRC Volume, URT Volume, Tidal Volume, and Breathing Frequency are modified to account for age (all other parameters remain constant across the age groups).

Table 10. MPPD parameters used in human simulations

Airway Morphology:	
FRC Volume (mL)	3300 (adult), 18.60 (3 mo), 55.92 (21 mo), 40.34 (23 mo), 33.41 (28 mo), 57.46 (3 yr), 740.42 (8 yr), 1029.24 (9 yr), 1314.81 (14 yr), 1636.7 (18 yr), 2792.57 (21 yr)
URT Volume (mL)	50 (adult), 2.45 (3 mo), 6.52 (21 mo), 6.94 (23 mo), 7.92 (28 mo), 9.47 (3 yr), 21.03 (8 yr), 22.44 (9 yr), 30.63 (14 yr), 37.38 (18 yr), 42.27 (21 yr)
Breathing Route	Nasal
Breathing Parameters:	
Tidal Volume (mL)	625 (adult), 30.44 (3 mo), 81.22 (21 mo), 86.79 (23 mo), 100.1 (28 mo), 121.3 (3 yr), 278.2 (8 yr), 295.8 (9 yr), 388.1 (14 yr), 446.7 (18 yr), 477.2 (21 yr)
Breathing Frequency (breaths/min)	12 (adult), 39 (3 mo), 28 (21 mo), 27 (23 mo), 26 (28 mo), 24 (3 yr), 17 (8 yr), 17 (9 yr), 16 (14 yr), 15 (18 yr), 14 (21 yr)
Inspiratory Fraction	0.5
Pause Fraction	0
Acceleration of Gravity (cm/s^2)	981
Body Orientation	Upright
Particle Properties:	
Diameter Designation	Count Mean Diameter (CMD)
Density (g/cm^3)	1
Particle Aspect Ratio	1 (spherical)
Nanoparticle model?	No
Insoluble?	Yes
Hygroscopic?	No
Geometric Standard	1

Deviation	
Aerosol Concentration (mg/m^3)	1
Inhalability Adjustment?	Yes

Figure 2 shows the results of the MPPD predictions for head deposition fraction as a function of particle size and age. One striking observation from Figure 2 is that for all particle sizes except the smallest (i.e., 1 µm), the adult, 21 year old, and 18 year old exhibit a larger head deposition fraction compared to the rest of the ages considered, with this difference being most pronounced for particle sizes in the 3 – 15 µm range. Another interesting result is that the head deposition fraction curves for the adult, 21 year old, and 18 year old look qualitatively similar in shape, and the head deposition fraction curves for the 3 month old through 14 year old look qualitatively similar in shape. However, in general, the 18 year old – adult curves do not look qualitatively similar to the 3 month old – 14 year old curves besides the fact that both sets of curves generally increase to a local maximum then decrease.

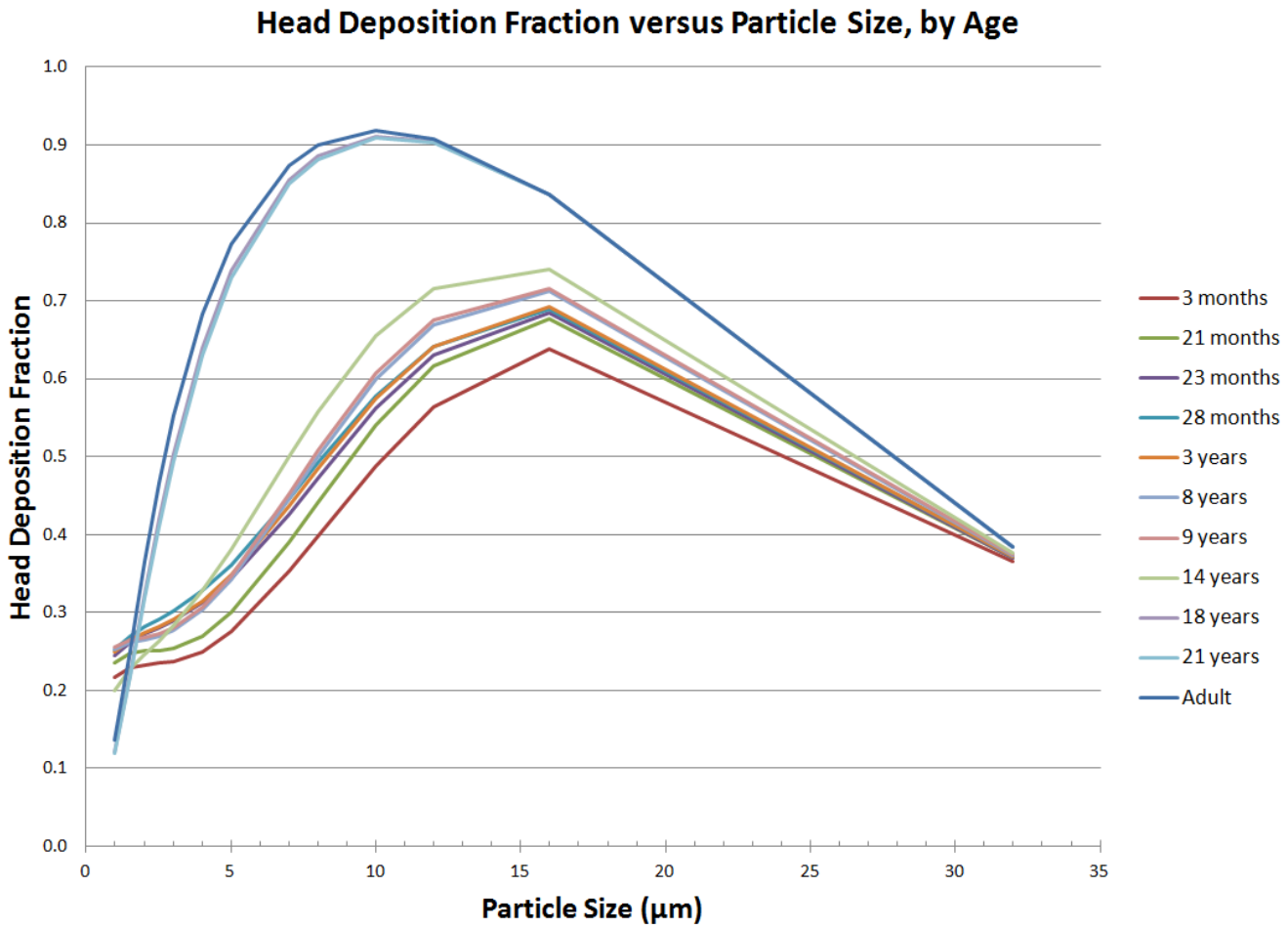

Figure 2. MPPD predictions of head deposition fraction as a function of particle size and age

Figure 3 shows the results of the MPPD predicted tracheobronchial deposition fraction versus particle size and age. As with the head deposition curves, there are again distinct groupings by age in that the 18 year old – adult curves look qualitatively similar and in general are grouped together, and the 3 month old – 14 year old curves look qualitatively similar and in general are grouped together. However, a distinct difference from the head deposition curves is that for the tracheobronchial deposition curves, the 18 year old – adult now tends to have a lower deposition fraction (except for particle sizes < 3 µm) compared to the 3 month old - 14 year old. Another observation from Figure 3 is that the 3 month old and 21 month old in general have significantly higher tracheobronchial deposition fractions compared to the rest of the age groups, especially in the 3 – 15 µm particle size range. A final observation is that for particle sizes greater than approximately 16 µm, there is still significant deposition in the tracheobronchial region for the 3 month old – 14 year old, whereas the tracheobronchial deposition fraction for the 18 year old – adult is essentially zero.

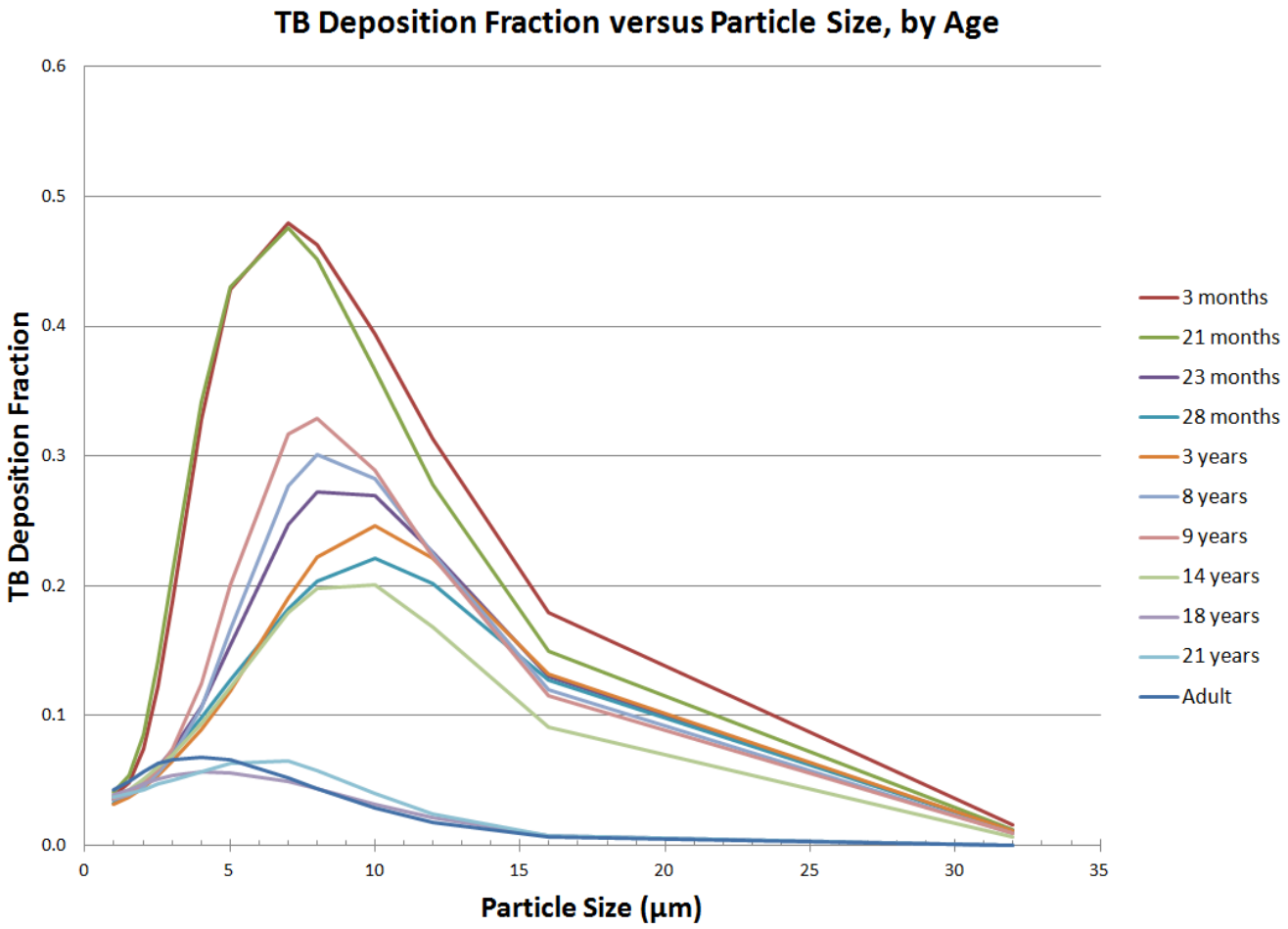

Figure 3. MPPD prediction of tracheobroncial deposition fraction as a function of particle size and age

Figure 4 shows the results of the MPPD prediction of pulmonary deposition fraction versus particle size and age. This figure exhibits a different trend than the previous two figures in that instead of there being different groupings, all curves for pulmonary deposition look qualitatively similar. Another observation is that no clear generalizations based on age may be made, besides the fact that the 8 and 9 year olds exhibit the highest local maximum of pulmonary deposition fraction around a particle size of 4 µm, and that the adult exhibits the lowest local maximum of pulmonary deposition fraction. One final observation from Figure 4 is that for all ages, the pulmonary deposition fraction is essentially zero for particle sizes greater than 16 µm.

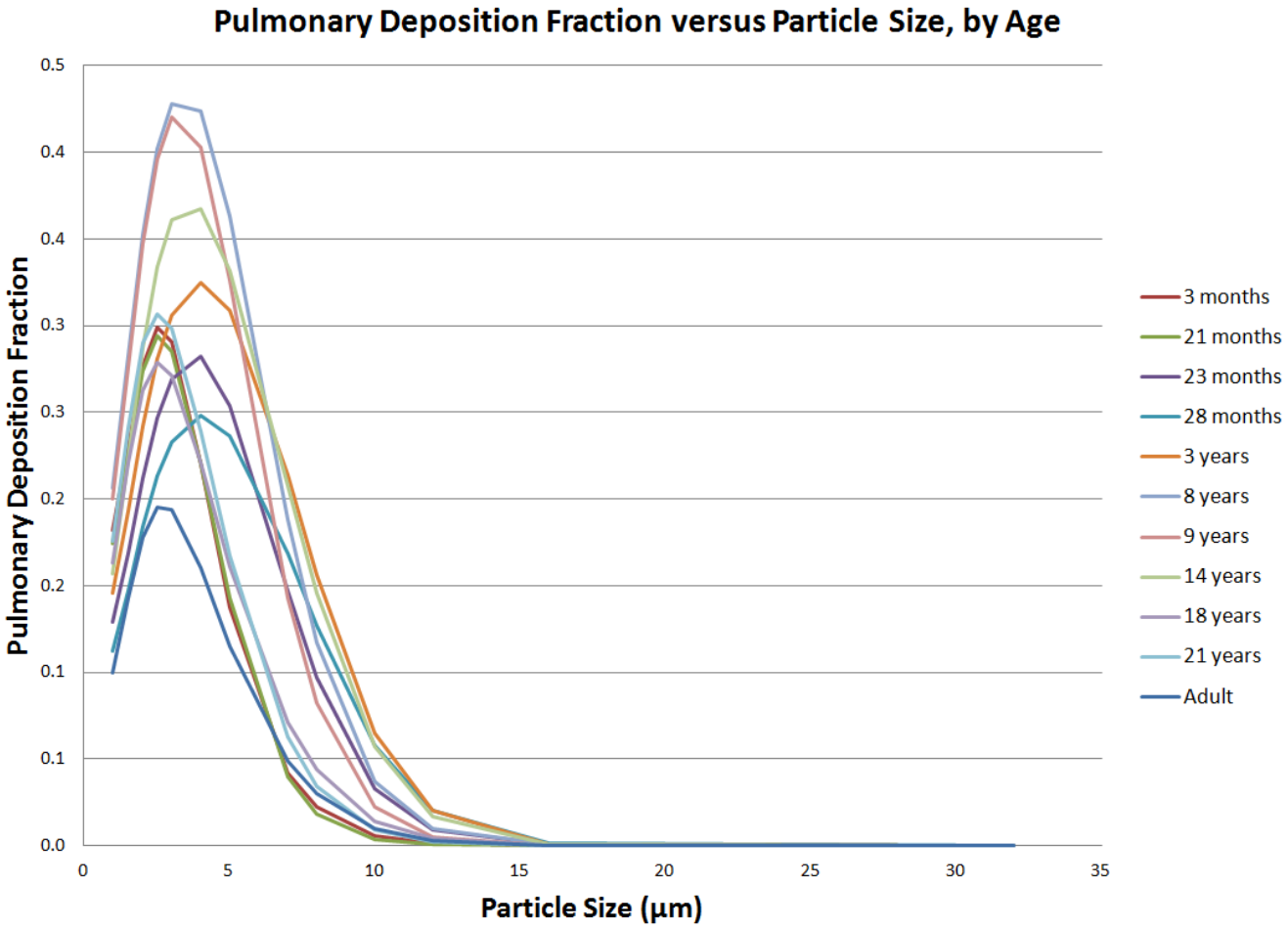

Figure 4. MPPD prediction of pulmonary deposition fraction as a function of particle size and age

11.3. APPLICATION TO CASUALTY ESTIMATION SCENARIOS

When considering application of demographic variability of inhalation mechanics to casualty estimation scenarios, the baseline effect that must be considered is that demographic factors, whether one or many, will in the end alter the deposition pattern of particles in the lung. Both total deposition and deposition by region will be different for different demographic members given the same exposure to an agent.

When modeling the effects of agent exposure on a person, there are varying levels of detail that may be prescribed. Some models of agent infectivity simply consider presented dose (sometimes referred to as exposure or inhaled dose), without regard to deposition of that dose within the body. For example, NATO Report AMedP-8(C) (81) contains a model for anthrax infectivity based upon the number of spores to which a person is exposed. An improved model will consider the fact that infection from an agent can only occur if the agent deposits in a specific region (head, tracheobronchial and/or pulmonary) in sufficient quantity. Such considerations are agent-dependent. For example, in the current version of the code FXCODA (82), the bacteria *Franciscella tularensis* is assumed to cause a tularemia infection only if it deposits in sufficient

quantities in the upper respiratory and/or pulmonary region (i.e., tracheobronchial deposition is neglected).

As a toy example of how the demographic variable of age may affect casualty predictions, consider Figure 5, which shows MPPD predictions of total deposition versus age and particle size, normalized by the adult value. The purpose of the normalization is to show how the age groups other than adult compare to the adult value. For example, if a curve for a particular age at a particular particle size lies below the adult curve (which is constant at 1), then the deposition for that age is less than the adult deposition, and vice versa.

Now, consider a hypothetical situation where a population is attacked with a pathogen of particle size 3 μm which requires a certain number of total deposited particles to cause infection. Furthermore, assume that all members of the population receive the same presented dose, and that in the adult, the total deposited dose, given the presented dose, is sufficient to cause 50% infection. By observation of Figure 5, it is seen that for 18 and 21 year olds, the total deposited dose is expected to be greater than the adult (even though the presented dose was the same), which means that these two age groups would be expected to have an infection rate greater than 50% (assuming no factors other than total deposition affect the infection rate). Conversely, for the 3 month old – 14 year old age groups, the total deposited dose is less than compared to the adult (again, even though the presented dose was the same), which means that these other age groups would be expected to have an infection rate less than 50% (with the 28 month old age group expected to exhibit the lowest infection rate due to the lowest total deposition). Overall, the implication from this toy example is that a casualty estimation program that does not account for age will assume that the entire population will be infected at a rate of 50%, whereas in reality the rate will be less than 50% overall if age is taken into consideration, which will drive consequence assessment.

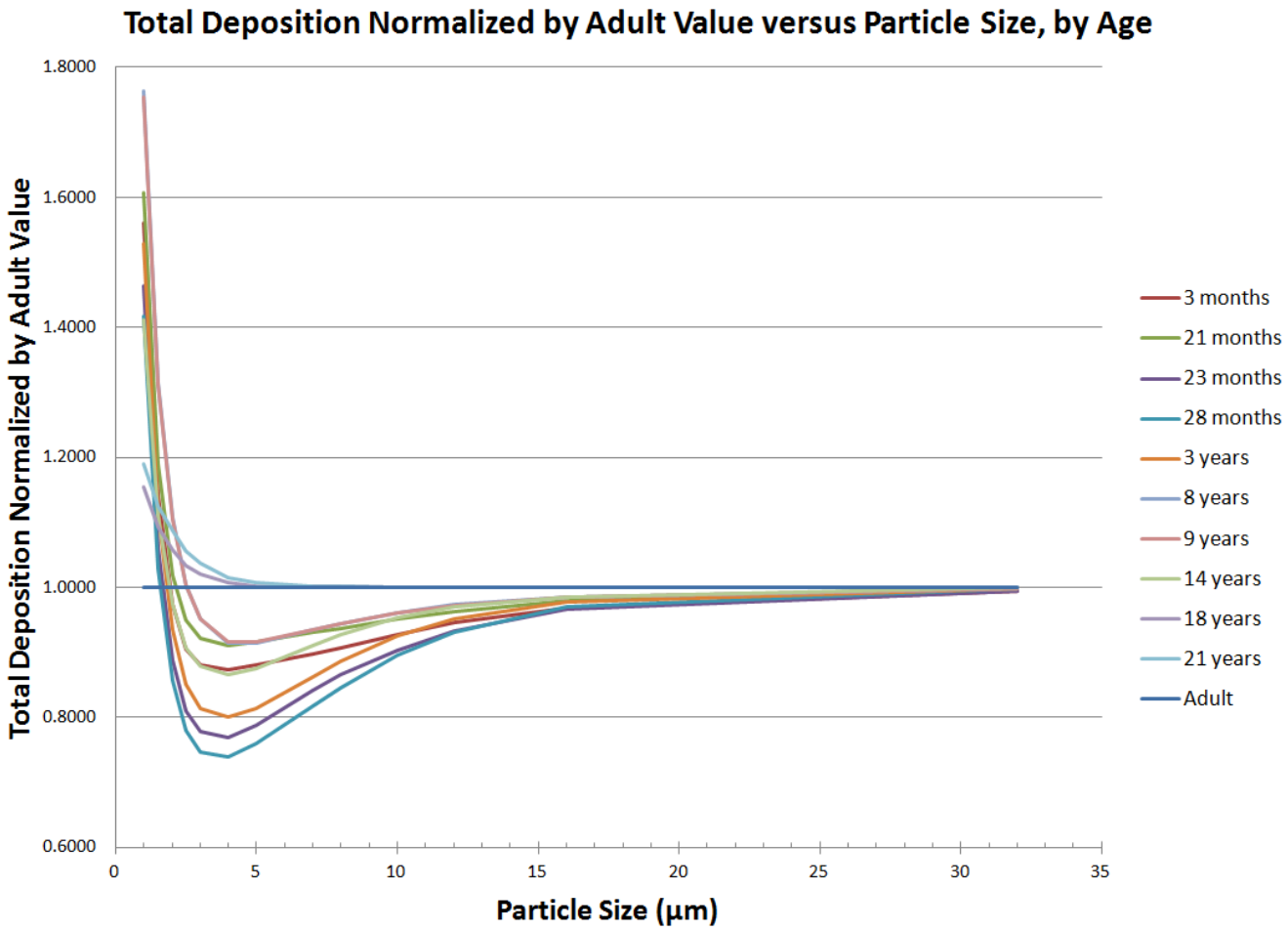

Figure 5. MPPD prediction of total deposition versus age and particle size, normalized by the adult value

In order to utilize the multiple age group models available in MPPD when calculating casualty estimates for a population, population data concerning the age breakdown of the population will be required. The U.S. Census Bureau publishes demographic data for the United States, with the principal demographic factors of age, gender, and ethnicity considered. Table 11, which shows the 2010 U.S. Census Data for the age breakdown of the U.S. population, is an example of such data available (80). Table 11 is an abbreviated summary of the data; a much more detailed breakdown (such as by intervals of one year of age) is also available, and should be utilized when matching MPPD ages available to the general population. One important point to be made is that Table 11 illustrates that the multiple age breakdowns available in MPPD for age 21 years and younger represent approximately 1/3 of the entire U.S. population. So, significant advances in prediction accuracy may be made by accounting for the younger 1/3 of the U.S. population that possesses inhalation mechanics parameters significantly different from those of the adult.

Table 11. 2010 U.S. Census data for age of the U.S. population (80)

Age Group	Percent of U.S. Population
Under 5 years old	6.94
5 to 9 years old	6.71
10 to 14 years old	6.51
15 to 19 years old	7.02
20 to 24 years old	7.02
25 years and older	65.8

The U.S. Census Bureau also publishes demographic data for major metropolitan areas. It stands to reason that some cities may have younger (or older) populations than other cities, so accounting for this effect will also result in more accurate modeling and prediction of casualty estimates compared to using the generic U.S. cross-section of the population. Table 12 shows statistics related to select metropolitan statistical areas in the United States; the metropolitan statistical areas with the highest and/or lowest percentages in any given category have been explicitly included in the table.

Table 12. U.S. Census age data for representative metropolitan areas (80)

Metropolitan Statistical Area (Highest/Lowest % in U.S. if Applicable)	Percent Under 18 Years	Percent Between 18 – 65 Years	Percent 65 Years and Older
Washington-Arlington-Alexandria, DC-VA-MD-WV	24.4	65.6	10.0
Tampa-St. Petersburg-Clearwater, FL (Tie-Highest % 65 Years and Older)	21.6	61.2	17.2
Pittsburgh, PA (Tie-Highest % 65 Years and Older) (Lowest % Under 18 Years)	20.2	62.6	17.2
El Paso, TX (Highest % Under 18 Years)	31.4	58.0	10.6
Austin-Round Rock, TX (Lowest % 65 Years and Older)	25.2	66.9	7.9
Los Angeles-Long Beach-Santa Ana, CA	25.3	63.9	10.8
Boston-Cambridge-Quincy, MA-NH	21.7	65.4	12.9

12. CONCLUSION

This report has reviewed a variety of factors concerning demographic variability of inhalation mechanics. The major demographic factors that influence inhalation mechanics are age, gender, body size and height, ethnicity, smoking, altitude, pregnancy, and lung disease.

To enhance existing inhalation and respiratory mechanics models to account for population demographic variables, the most straightforward approach will be to first consider what respiratory mechanics parameters (such as lung volume and tidal volume) exhibit different values based on demographic considerations. This approach will involve a careful exploration and compilation of the references covered in this report to determine how these variables change based on demographics. Once these changes are determined, they may be implemented in respiratory mechanics models.

There are specific updates to existing DoD software that may be made by considering demographic variability of inhalation mechanics. Specifically, the Hazard Prediction and Assessment Capability (HPAC) program uses deposition predictions from MPPD to predict mortality rates from exposure to *Franciscella tularensis* and ricin. Currently, only adults are considered in HPAC, which may not be ideal for a typical civilian population (but is appropriate for a military population). Since MPPD already implements age-specific models (from 3 months to 21 years old), the deposition patterns and subsequent mortality rates due to infection may be determined by age using MPPD. Such a distinction is important because children and adults will exhibit different deposition patterns given the same aerosol challenge, and will therefore be expected to experience different mortality rates. Furthermore, when using census or other similar data to determine the division of the population by age, a more robust casualty prediction due to a biological attack for a civilian population may be made by incorporating this data.

One gap that is present in the literature is a large body of experimental studies correlating deposition with demographic factors, although some do exist. Although models such as MPPD may be used to predict deposition once the differences in respiratory variables are accounted for, full validation will require comparison to experiment.

13. WORKS CITED

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14. DEFINITIONS, ACRONYMS, AND ABBREVIATIONS

ARA	Applied Research Associates, Inc
COPD	Chronic Obstructive Pulmonary Disease
DoD	Department of Defense
DTRA	Defense Threat Reduction Agency
ERV	Expiratory Reserve Volume
FEF	Forced Expiratory Flow
FEV	Forced Expiratory Volume
FVC	Forced Vital Capacity
FRC	Functional Residual Capacity
HPAC	Hazard Prediction and Assessment Capability
IC	Inspiratory Capacity
IRV	Inspiratory Reserve Volume
JEM	Joint Effects Model
JOEF	Joint Operation Effects Federation
JPEO-CBD	Joint Program Executive Office for Chemical/Biological Defense
JPM-IS	Joint Program Manager-Information Systems
JSTO	Joint Science and Technology Office
MEF	Maximum Expiratory Flow
MPPD	Multiple-Path Particle Dosimetry Model
MV	Minute Volume
PEF/PEFR	Peak Expiratory Flow / Peak Expiratory Flow Rate
RV	Residual Volume
TV	Tidal Volume
TLC	Total Lung Capacity
URT	Upper Respiratory Tract Volume
VC	Vital Capacity

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